

Rolf Sköld

**THERMOCHEMICAL STUDIES ON AQUEOUS
SOLUTIONS OF BIOCHEMICAL MODEL COMPOUNDS**

WITH PARTICULAR EMPHASIS ON PARTIAL MOLAR HEAT CAPACITIES



Lund 1976



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This review gives a summary of results from the following papers which will be referred to by Roman numerals I-V.

- I. N. Nichols, R. Sköld and I. Wadsö
Testing of an Automatic Temperature Recording System for an Isoperibolic Solution Calorimeter.
Chemica Scripta. In press.
- II. G. Öjelund, R. Sköld and I. Wadsö
Thermochemistry of Solutions of Biochemical Model Compounds.
5. Transfer of N-alkylamides from Water to Non-aqueous Media.
J. Chem. Thermodynamics 1976, 8, 45.
- III. N. Nichols, R. Sköld, C. Spink and I. Wadsö
Thermochemistry of Solutions of Biochemical Model Compounds.
6. α, ω -diols, -diamines and -dicarboxylic acids in Aqueous Solution.
J. Chem. Thermodynamics. Submitted.
- IV. R. Sköld, J. Suurkuusk and I. Wadsö
Thermochemistry of Solutions of Biochemical Model Compounds.
7. Aqueous Solutions of Some Amides, t-Butanol and Pentanol.
J. Chem. Thermodynamics. Submitted.
- V. N. Nichols, R. Sköld, C. Spink, J. Suurkuusk and I. Wadsö
Additivity Relations for the Heat Capacities of Nonelectrolytes in Aqueous Solution.
J. Chem. Thermodynamics. Submitted.

INTRODUCTION

As a result of a large amount of experimental and theoretical efforts aimed at explaining the nature of water and aqueous solutions, a number of models have been proposed regarding the structure of this ubiquitous liquid and the influence of solutes on its structure. References are given in several comprehensive reviews dealing with this subject (1-3).

Even if none of the current models have been shown to explain unambiguously all the particular properties displayed by aqueous systems, the most widely adopted ideas agree upon a model with water molecules partaking to different extents in four-coordinated hydrogen bonded lattices. Molecules not employing all possibilities of hydrogen bonding are believed to comprise within the liquid a denser "phase" than the bulky structure, which results from the three-dimensional network formed by extensively hydrogen bonded species. A solute molecule introduced in water is accordingly classified as either structure-promoting or structure-breaking, depending on whether it causes a shift in the equilibrium towards a state of higher or lower degree of coordination, respectively.

From studies of temperature effects on solubilities, it has been found that solvation of nonpolar molecules in water is characterized by an entropy decrease of the system, more than outweighing the small but mostly exothermic enthalpy change accompanying the process, thus making the free energy change unfavorable (reference 2, p. 16). Since the solvation of molecules which are not capable of compensating for the broken or distorted water-water hydrogen bonds would be expected to result in positive enthalpy changes, the exothermic enthalpies and negative entropies of solvation obtained experimentally are generally interpreted as originating from a higher degree of structuring in the vicinity of the solute molecule.

Recognition of the importance of the entropy term as the major driving force in processes involving hydrophobic interactions in water, has been essential for the present understanding of factors governing three-dimensional stability in biochemical systems like those formed by proteins or by amphiphilic aggregates in aqueous solution (1-5). The increased structural rigidity of liquid water imposed by the presence of non-polar solutes, is also indicated by an anomalous temperature dependence of the enthalpy of solution. This phenomenon is believed to be related to the breakdown of excess water structure with increasing temperature. Limiting partial molar heat capacities do not include any lattice contributions from the pure compounds and therefore reflect more directly solute-solvent interactions, and the same is pertinent to thermodynamic properties for the transfer of solutes at infinite dilution between different solvents, even if the situation in the latter case is somewhat more complex. The present summary is largely devoted to the study of thermodynamic properties of some non-ionic compounds which can be regarded as simple models for the behaviour of biomolecules in aqueous solutions.

Paper II reports the results of a systematic investigation of enthalpies of transfer at infinite dilution for some N-alkylamides in solvents of varying polar characters. For N-butylacetamide, enthalpies of solution were determined at three different temperatures from which heat capacities of solution and transfer were obtained.

Partial molar heat capacities in water at infinite dilution is the main issue of paper III which deals with a series of α,ω -diols, -diamines and -dicarboxylic acids, while paper IV presents values for the same thermodynamic property for some amides, t-butanol and n-pentanol. For most of the compounds included in papers III and IV, enthalpies of solution at infinite dilution and heat capacities for the pure compounds have been determined.

In paper V is presented a systematic survey of values available for the partial molar heat capacities for simple non-ionic compounds in dilute aqueous solution. An empirical additivity scheme is worked out for the contributions from different functional groups to the limiting aqueous partial molar heat capacities. The scheme is founded on several series of compounds of the type $H-(CH_2)_n-X$ and allows some qualitative conclusions to be drawn regarding the relative effects of different atomic or group substituents on the interactions with liquid water. Observed deviations between empirically derived and experimental values for some other types of compounds, suggests that further studies of these substances in aqueous solution is needed.

An automatic temperature recording system used with an isoperibolic solution and reaction calorimeter is described and tested in paper I. The calorimeter and most parts of the set-up are essentially identical to those of the LKB 8721-1 instrument, but the present system does not make use of a balanced Wheatstone-bridge for the temperature measurements. The performance of the instrument has been tested with the TRIS-HCl test reaction. The calorimeter has been used in connection with the work reported in papers III and IV.

Symbols and abbreviations. In the following text molar enthalpies and heat capacities of solution at infinite dilution and the quantities for the corresponding transfer process will be denoted ΔH_{soln}^∞ , $\Delta C_{p,soln}^\infty$, $\Delta H_{transfer}^\infty$ and $\Delta C_{p,transfer}^\infty$, respectively. C_p^* stands for the molar heat capacity of the pure compound while $C_{p,2}^\infty$ is the symbol used for solute partial molar heat capacities at infinite dilution. TRIS is the short form for tris(hydroxymethyl)amino-methane. For experimental conditions and equations used reference is given to papers I-V.

TESTING AN AUTOMATIC TEMPERATURE RECORDING SYSTEM FOR AN ISOPERIBOLIC SOLUTION CALORIMETER (Paper I)

The instrumental array is shown schematically in Figure 1. The voltage over the thermistor, induced by the passage of a constant current, is amplified after compensation of the major part of the signal and read by a five-place digital voltmeter. During an experiment, readings are usually taken every five seconds and printed on paper tape. No attempts were made to optimize the performance of the instrument, e.g. by systematic investigation of the effect of variation of parameters such as thermistor current and amplification, but conditions are similar to those applying for the commercial LKB 8721-1 instrument (6).

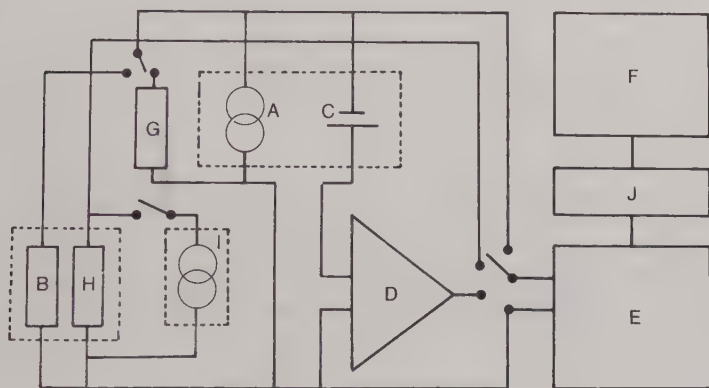


Figure 1. Schematic drawing of temperature measurement and data acquisition system. A = constant thermistor current supply. B = thermistor. C = compensation potential source. D = amplifier. E = digital voltmeter. F = tape punch. G = dummy resistance. H = calibration heater. I = calibration current source. J = interface unit.

Analysis of data obtained from simulated experiments, experimental precision for small heat effects and the precision shown in calibration experiments indicate a practical sensitivity for temperature changes in the order of $2 \cdot 10^{-5}$ K. The two methods employed to evaluate the temperature effect of heat exchange with the surroundings (7) seem to lead to small differences in the calculated temperature changes, but when ΔH_{soln} values were calculated using the two separate sets of ΔT values, differences were found to be random and insignificant. With small heat effects the differences were similar but insignificant as shown in Table 1.

Table I. Electrical calibration experiments^a

Series	P/W	Q/J	$\Delta T/K$	$\bar{\epsilon}_{RP}/J\ K^{-1}$	$\bar{\epsilon}_D/J\ K^{-1}$
1	0.6	127	0.29	441.94 ± 0.01	442.02 ± 0.02
2	0.4	46	0.10	444.38 ± 0.19	444.47 ± 0.15

^a $\bar{\epsilon}_{RP}$ and $\bar{\epsilon}_D$ are mean values for effective heat capacities calculated from a series of calibration experiments employing the methods of Regnault-Pfandler and Dickinson, respectively.

Weighted mean values for the results from TRIS-HCl test experiments are $\Delta H_{soln} = -(30.632 \pm 0.008)$ at 293.15 K, $\Delta H_{soln} = -(29.768 \pm 0.003)$ at 298.15 K and $\Delta H_{soln} = -(28.893 \pm 0.007)$ kJ·mol⁻¹ at 303.15 K.

The value at 298.15 K is slightly higher than results of most series of measurements previously obtained with the LKB instrument (8-10). However, when possible systematic and random errors are considered there appears to be no significant difference. It is thus concluded that the simple automatic method for temperature measurement is as precise and accurate as the method involving a manually operated resistance bridge.

The estimated probable systematic error is ± 0.012 kJ·mol⁻¹ (11) and the factors considered are given in Table 2.

Table 2. Systematic errors

Source of systematic error	Estimated fractional error in ΔH_{soln}
U_n^a	$4 \cdot 10^{-5}$
Time of heating: t	10^{-4} (instrument specification)
Assigned effective heater	
resistance: R_{eff}	$2 \cdot 10^{-4}$
ΔT_{soln}^b	$7 \cdot 10^{-5}$
ΔT_{cal}^b	$7 \cdot 10^{-5}$
Determination of absolute	
temperature: T_{abs}	$6 \cdot 10^{-5}$
Mass determination: m	$5 \cdot 10^{-5}$
Vaporization and bulb breaking: V-B	$6 \cdot 10^{-5}$

a) potential measured across the calibration heater in connection with each experiment.

b) corrected temperature changes in solution and calibration experiments, respectively.

ΔH_{soln} values are calculated from

$$\Delta H_{\text{soln}} = \left(\frac{U_n}{R_{\text{tot}}} \right)^2 \cdot \text{Reff} \cdot t \cdot \frac{\Delta T_{\text{soln}}}{\Delta T_{\text{cal}}} \cdot \frac{M}{m} + \Delta C_{p_{\text{soln}}} \cdot \Delta T_{\text{abs}} + \Delta H_{V-B}$$

where R_{tot} is heater resistance including leads, M is molecular weight of TRIS, ΔT_{abs} stands for correction to nominal temperature of the reaction and ΔH_{V-B} is an enthalpy correction term including heat of vaporization and heat of bulb breaking. For other symbols see Table 2. A maximum estimated error from these data would be $\pm 0.020 \text{ kJ}\cdot\text{mol}^{-1}$.

The obtained value for ΔH_{soln} at 298.15 K compares excellently with the NBS certified value (12), $\Delta H_{\text{soln}} = -(29.771 \pm 0.031) \text{ kJ}\cdot\text{mol}^{-1}$, and like Prosen et al. (12, 13) it was found that a linear relationship was adequate to describe the temperature dependence of ΔH_{soln} . The determined $\Delta C_{p_{\text{soln}}}$ value at 298.15 K, $\Delta C_{p_{\text{soln}}} = (173.9 \pm 1.3) \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$, is also in very good agreement with the value established by the NBS workers, $\Delta C_{p_{\text{soln}}} = (173.8 \pm 2.8) \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$. Prosen and Kilday found, however, some varying thermal effects depending on whether the calorimeter was closed or open to the air, and suggested that a side reaction with CO_2 or O_2 might be responsible for the more exothermic values obtained in the presence of the gases. This unknown effect was partly the cause of the relatively large uncertainty which they ascribed to the certified value.

In order to investigate the effect of CO_2 on ΔH_{soln} a series of investigations were undertaken in the present work where CO_2 was bubbled through the HCl solution for 2 h before it was charged into the calorimeter. Alternating with these measurements experiments were performed under standard conditions without CO_2 -gassing. For the standard experiments a normal value for ΔH_{soln} was obtained while a slightly lower value was found in the presence of CO_2 . The effect may well be due to evaporation of CO_2 caused by the temperature increase during an experiment. From test experiments carried out in a closed bomb calorimeter, Olofsson et al. (14) obtained a normal value.

These experiments thus give no reason to suspect the presence of any exothermic side reaction in the TRIS-HCl system.

THERMOCHEMISTRY OF TRANSFER OF SOME N-ALKYLAMIDES FROM WATER TO NON-AQUEOUS MEDIA (Paper II)

In many enzymatic reactions the first step is a diffusion process where the reactant is transferred from an aqueous environment to a site in the protein molecule with the result that parts of the reactant and protein will be exposed differently to the aqueous phase. The importance of such medium effects are well appreciated and one way of obtaining information about the thermodynamic quantities involved is by studying effects of solute-solvent interactions in model systems. In paper II low molecular weight amides are used as simple models for compounds containing peptide links.

$\Delta H_{\text{soln}}^{\infty}$ values were determined at 298.15 K for several amides in MeOH, EtOH, PrOH and CCl_4 . For BuNHCOMe, $\Delta H_{\text{soln}}^{\infty}$ in MeOH, EtOH and CCl_4 was measured at three temperatures and the corresponding $\Delta C_{p,\text{soln}}^{\infty}$ values were calculated. For most of the amides, values for $\Delta H_{\text{soln}}^{\infty}$ and $\Delta C_{p,\text{soln}}^{\infty}$ in H_2O and Cp^* was available from an earlier study (15). In the polar solvents, $\Delta H_{\text{soln}}^{\infty}$ values were easily obtained but in CCl_4 amides were found to be extensively associated even in dilute solutions. In order to make proper extrapolations to infinite dilution, association constants were evaluated spectrophotometrically by applying an analysis as described in references 16 and 17. From the derived association constants and results of calorimetric solution experiments, enthalpies for breaking of interamide hydrogen bonds, ΔH_{H} , were calculated using a two-step model for the solution process.

By use of a flow microcalorimeter enthalpies of dilution, ΔH_{diln} , of BuNHCOMe in CCl_4 were measured over a wide concentration range and the results of these experiments were used to estimate another value for ΔH_{H} using the association constants from spectrophotometric experiments. Another approach is to minimize the sum of errors in ΔH_{H} from the different dilution experiments by varying the association constants in equation 16 of paper II. Association constants thus obtained are in good agreement with spectrophotometric results.

Peptide hydrogen bonding is an important factor for the stabilization of secondary protein structure and has been investigated in several publications. Association constants and ΔH_{H} values for BuNHCOMe from this study are compared to values for other amides in Table 3.

Transfer enthalpies are summarized in Table 4 and it can be seen that there is a substantially positive $\Delta H_{\text{transfer}}^{\infty}$ from H_2O to MeOH and, with the exception of the rather low value for OctNHCOMe, the values are similar in magnitude. For the transfer between alcohols with increasing hydrocarbon chain lengths, enthalpy changes are small. Finally, for the transfer from alcohols to CCl_4 there is again a large positive $\Delta H_{\text{transfer}}^{\infty}$ value. Transfer of monomeric short chain N-alkylamides from H_2O to CCl_4 appears to be associated with an almost constant enthalpy change the mean value being, $\Delta H_{\text{transfer}}^{\infty} = (31 \pm 1) \text{ kJ} \cdot \text{mol}^{-1}$. No correlation between structure and $\Delta H_{\text{transfer}}^{\infty}$ can be discerned from the values in the table.

In Table 5 are given $\Delta C_{p,\text{soln}}^{\infty}$ and $C_{p,2}^{\infty}$ values for Bu NHCOMe in various solvents. The high $C_{p,2}^{\infty}$ value in water is from paper IV and is the expected result of interaction between hydrophobic parts of the molecule and H_2O . For the alcohol solution $C_{p,2}^{\infty}$ values are nearly identical to Cp^* , while a positive $\Delta C_{p,\text{soln}}^{\infty}$ value is found in CCl_4 . There are indications in the literature that this effect is due to a temperature dependent position of the cis-trans equilibrium of the amide in non-polar solvents (25) even if results of dipole-moment investigations in reference 26 seem to exclude this possibility for MeNHCOMe in CCl_4 .

TABLE 3. Self-association constants and ΔH_H values for some N-alkylamides in CCl_4 .

Amide	Method	Temp/ $^{\circ}C$	K_2	K_3	$\Delta H_H/kJ\ mol^{-1}$	Ref.
Me-NHCO-Me	ir	25	4.7(5.8) ^a	-	-17.6	17
"	"	26	5.4	-	-19.7	18 ^b
"	"	25	1	38	-19.7	19
"	v.p.	20	9	61.6	-	20
"	cal	25	25 $\pm$ 3	-	-21.1(-25.9) ^a	21
"	"	"	15.4	"	-22.6	22
"	nmr	"	1.55 $\pm$ 0.06	24.7 $\pm$ 0.9	-15.5 $\pm$ 1.3 ^c	23
Et-NHCO-Me	cal	"	13.8	-	-20.9	22
Me-NHCO-Et	"	"	11.3	-	-19.5	22
i-Pr-NHCO-Me	nmr	"	1.02 $\pm$ 0.04	16.4 $\pm$ 1.3	-12.6 $\pm$ 1.3 ^c	23
"	"	"	1.5 $\pm$ 0.2	14.5 $\pm$ 1	-	24
t-Bu-NHCO-Me	"	25	0.66 $\pm$ 0.30	6.1 $\pm$ 0.1	-10.0 $\pm$ 0.8 ^c	23
Bu-NHCO-Me	fl. cal, ir	"	1.4 $\pm$ 0.2	24.1 $\pm$ 1	-19.8 $\pm$ 0.6	Paper II
	s. cal, ir	"	"	"	-23.5 $\pm$ 3.4	"
	fl. cal	"	1.35	23.0	-19.4 $\pm$ 0.6	"

^a determined by two different methods of analysis. ^b assuming only monomer-dimer equilibrium. ^c these ΔH_H values refer to the monomer-dimer equilibrium. For larger aggregates Graham and Chang derived the values -18.8, -18.0 and -13.8 kJ mol⁻¹, respectively, for Me-NHCO-Me, i-Pr-NHCO-Me and t-Bu-NHCO-Me.

Table 4. Enthalpies of transfer for some amides between different solvents at infinite dilution (25 °C, kJ mol⁻¹)

Amide	Solvent				
	H ₂ O	→	MeOH	→	EtOH → ProOH → CCl ₄
Me-NHCO-Me	12.73		-		-
Pr-NHCO-Me	14.97		0.70		-0.21 14.66
i-Pr-NHCO-Me	15.86		0.85		-0.33 16.30
Bu-NHCO-Me	14.40		0.46		16.60
t-Bu-NHCO-Me	13.05		0.34		-0.38 16.37
Et-CONH-Me	14.64		0.76		14.57
i-Pr-CONH-Me	15.69		0.38		-0.18 16.17
t-Bu-CONH-Me	16.24		0.50		-0.10 14.44
Oct-NHCO-Me	7.32		-		-
Me-CONH-CH ₂ -CONH-Me	14.75		3.20		-

Table 5. $\Delta C_{p,2}^{\infty}$ and $C_{p,2}^{\infty}$ for BuNHCOMe at 298.15 K

Solvent	$\Delta C_{p,2}^{\infty} / \text{J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1}$	$C_{p,2}^{\infty} / \text{J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1}$
H ₂ O	280 ± 2 ^a	516 ± 1 ^b
MeOH	0 ± 2	236 ± 2
EtOH	-4 ± 6	232 ± 6
CCl ₄	81 ± 19	317 ± 19

^a From C_p^* in reference 15 and $C_{p,2}^{\infty}$ from paper IV

^b Paper IV

THERMOCHEMISTRY OF AQUEOUS SOLUTIONS OF BIOCHEMICAL MODEL COMPOUNDS (Papers III and IV)

In paper III is reported the results of calorimetric measurements of $\Delta H_{\text{soln}}^{\infty}$ in water at 293.15, 298.15 and 303.15 K for compounds of the type $X-(CH_2)_n-X$ where $n = 2-5$ for $X=OH$, $n = 2-4$ for $X=NH_2$ and $n = 2$ and 3 for $X=COOH$. From these results $\Delta C_{p,\text{soln}}^{\infty}$ values were calculated at 298.15 K. $C_{p,X}^{\infty}$ at 298.15 K was obtained using a drop heat capacity calorimeter (27) and by combination with $\Delta C_{p,\text{soln}}^{\infty}$ values, $C_{p,2}^{\infty}$ was calculated. $C_{p,2}^{\infty}$ values for 1,6-hexanediol and the dicarboxylic acids were determined by measuring the heat capacities of their aqueous solutions at different solute concentrations (28). The $C_{p,2}^{\infty}$ values for 1,2-ethane and 1,3-propanedicarboxylic acid from the two methods were found, within uncertainties, to be the same.

In paper IV $\Delta H_{\text{soln}}^{\infty}$ in water was determined at 298.15 K for formamide, N-methyl-formamide, acetamide and t-butanol and the corresponding $C_{p,2}^{\infty}$ values at 298.15 K were obtained for these compounds and for N-methylacetamide, N-butyl-acetamide, N-methylpentanamide and pentanol from the concentration dependence of the heat capacities of their aqueous solutions (28).

A concentration dependent $\Delta H_{\text{soln}}^{\infty}$ value was only noted for t-butanol (1). This effect can be caused by solute-solute interactions at low concentrations. Re-considering the heat capacity data of the aqueous solutions of t-butanol in terms of apparent heat capacities does not exclude this possibility, even if a concentration dependent apparent heat capacity may well result from a small systematic error in the heat capacity value used for the solvent (c.f. however the anomalously large $C_{p,2}^{\infty}$ value for t-butanol in water as discussed in paper V).

A value for the specific heat capacity of 0.100 mol·dm⁻³ HCl solution is reported, $C_p = (4.1534 \pm 0.0004) \text{ J} \cdot \text{K}^{-1} \cdot \text{g}^{-1}$, which is significantly higher than the value obtained from apparent molal heat capacity data given in reference 29, $C_p = 4.1517 \text{ J} \cdot \text{K}^{-1} \cdot \text{g}^{-1}$.

Results of the calorimetric determinations are summarized in Tables 6 to 8 together with results of previous studies. For the amides, a linear relationship was obtained when $C_{p,2}^{\infty}$ was plotted versus n as shown in Figure 2 where also compounds from other studies are included. With the α,ω -compounds a similar plot gives non-linear relations which is believed to reflect characteristic structural features for these compounds in aqueous solution (c.f. discussion in paper V).

TABLE 6. Enthalpies of solution in water at infinite dilution, $\Delta H_{\text{soln}}^{\infty}$, for some diols, diamines and dicarboxylic acids.

Substance	$\Delta H_{\text{soln}}^{\infty} / \text{kJ mol}^{-1}$		
	293.15K	298.15K	303.15K
$\text{HO}-(\text{CH}_2)_2-\text{OH}$	-7.06 ± 0.02	-6.87 ± 0.02	-6.62 ± 0.01
$\text{HO}-(\text{CH}_2)_3-\text{OH}$	-9.11 ± 0.02	-8.67 ± 0.02	-8.19 ± 0.02
$\text{HO}-(\text{CH}_2)_4-\text{OH}$	-11.18 ± 0.01	-10.46 ± 0.01	-9.69 ± 0.03
$\text{HO}-(\text{CH}_2)_5-\text{OH}$	-11.66 ± 0.03	-10.59 ± 0.01	-9.60 ± 0.02
$\text{H}_2\text{N}-(\text{CH}_2)_2-\text{NH}_2^{\text{a}}$	-31.80 ± 0.01	-31.78 ± 0.01	-31.68 ± 0.01
$\text{H}_2\text{N}-(\text{CH}_2)_3-\text{NH}_2^{\text{a}}$	-35.80 ± 0.01	-35.62 ± 0.03	-35.27 ± 0.02
$\text{H}_2\text{N}-(\text{CH}_2)_4-\text{NH}_2^{\text{a}}$	-37.04 ± 0.02	-36.60 ± 0.02	-36.00 ± 0.02
$\text{HOOC}-(\text{CH}_2)_2-\text{COOH}^{\text{b}}$	28.39 ± 0.03	$28.71 \pm 0.02^{\text{c}}$	29.14 ± 0.04
$\text{HOOC}-(\text{CH}_2)_3-\text{COOH}^{\text{b}}$	24.65 ± 0.04	25.09 ± 0.01	25.67 ± 0.02

^aValues refer to dilute NaOH solution, $c = 0.100 \text{ mol dm}^{-3}$.

^bValues refer to dilute HCl solution, $c = 0.100 \text{ mol dm}^{-3}$.

^cVanderzee et al. (30) have earlier reported the value $28.70 \pm 0.03 \text{ kJ mol}^{-1}$.

TABLE 7. Heat capacity values for some diols, diamines and dicarboxylic acids at 298.15 K.

Substance	$C_p^*/J\ K^{-1}\ mol^{-1}$	$\Delta C_p^{oo}/J\ K^{-1}\ mol^{-1}$	This work	$C_p^{oo}/J\ K^{-1}\ mol^{-1}$	Literature ^a
$HO-(CH_2)_2-OH$	149.7 ± 0.1	43 ± 2	193 ± 2		191.9 ± 0.1 , 201 ^b
$HO-(CH_2)_3-OH$	176.4 ± 0.1	93 ± 4	269 ± 4		263 ^b
$HO-(CH_2)_4-OH$	204.2 ± 0.1	150 ± 3	354 ± 3		346.8 ± 0.3
$HO-(CH_2)_5-OH$	233.2 ± 0.2	206 ± 6	439 ± 6		
$HO-(CH_2)_6-OH$			528 ± 8 ^c		521.6 ± 0.2
$H_2N-(CH_2)_2-NH_2$	172.6 ± 0.1	12 ± 2 ^d	185 ± 2 ^d		
$H_2N-(CH_2)_3-NH_2$	203.8 ± 0.2	52 ± 3 ^d	256 ± 3 ^d		
$H_2N-(CH_2)_4-NH_2$	236.3 ± 0.2	104 ± 4 ^d	340 ± 4 ^d		
$HOOC-(CH_2)_2-COOH$	153.6 ± 0.2	75 ± 6 ^e	229 ± 6 ^e	225 ± 4 ^f	
			223 ± 5 ^{c,e}		
$HOOC-(CH_2)_3-COOH$	174.4 ± 0.4	103 ± 6 ^e	277 ± 6 ^e	271 ± 4 ^f	
			267 ± 5 ^{c,e}		
$HOOC-(CH_2)_4-COOH$	195.9 ± 0.3		336 ± 10 ^{c,e}		
$HOOC-(CH_2)_5-COOH$	217.7 ± 0.5		410 ± 5 ^{c,e}		

^aReferences in paper III. ^bRefers to 303.15 K. ^cMeasured directly with drop heat capacity calorimeter.^dValues refer to $0.100\ mol \cdot dm^{-3}$ NaOH solution. ^eValues refer to $0.100\ mol \cdot dm^{-3}$ HCl solution. ^fWeighted mean value.

TABLE 8. $\Delta H_{\text{soln}}^{\infty}$, C_p^* and $C_{p,2}^{\infty}$ for some amides and alcohols at 298.15 K ^a

Compound	$\Delta H_{\text{soln}}^{\infty}/\text{kJ}\cdot\text{mol}^{-1}$		$C_p^*/\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$		$C_{p,2}^{\infty}/\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$	
	This work	Earlier work	This work	Earlier work	This work	Earlier work
HCONH ₂ (l)	2.03 ± 0.01	2.01 ± 0.04 2.03 ± 0.01	107.62 ± 0.04	108.1 ± 0.5	82 ± 1	
HCONHMe(l)	-7.083 ± 0.005	-7.14 ± 0.02	123.8 ± 0.2	126.1 ± 0.7	164 ± 2	
MeCONH ₂ (s)	9.74 ± 0.01	9.54 ± 0.13 9.644 ± 0.008	90.3 ± 0.2	/	160 ± 1	163.8 ± 1
MeCONHMe(l)		-13.09 ± 0.02	151.4 ^b	/	258 ± 3 ^c	236
MeCONHBu(l)		-14.72 ± 0.03		236 ± 1	516 ± 1	506 ± 5
BuCONHMe(l)		-15.03 ± 0.02	238.4 ± 0.1	229 ± 1	524 ± 4	515 ± 5
t-BuOH(l)	-17.44 ± 0.02	-17.46 ± 0.06 -17.31 ± 0.14	218.6 ± 0.5	225 219.0 ± 0.1 ^b	463 ± 6	484 ± 4 502 ± 17 464 ± 0.6
PeOH(l)		-7.82 ± 0.05	208.40 ± 0.08	209	530 ± 7	559 ± 22 523.8 ± 0.3

^aFor literature reference see paper IV.

^bExtrapolated value.

^cDetermined by Dr N. Nichols.

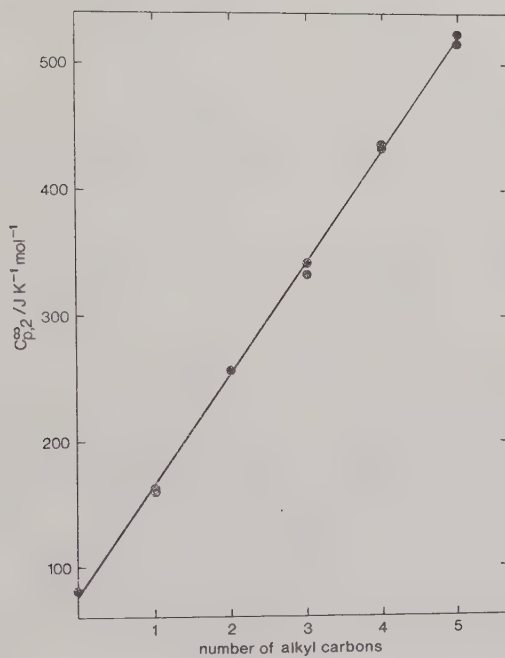


Figure 2. $C_{p,2}^{\infty}$ for some amides in aqueous solution at 298.15 K, plotted against number of alkyl carbons.

ADDITIVITY RELATIONS FOR THE AQUEOUS HEAT CAPACITIES OF NON-ELECTROLYTES (Paper V)

In paper V a simple additivity system is developed for contributions to aqueous $C_{p,2}^\infty$ from hydrogen and from functional groups comprising non-ionic molecules. Results from several calorimetric studies have been considered and it is shown that a linear relation holds for a plot of $C_{p,2}^\infty$ versus n for the different homologous series of the type $H-(CH_2)_n-X$ on which the system is based. Even in the step from $n=0$ to $n=1$ the mean CH_2 -increment is in most cases found to be close to the overall mean value, $90 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$, although it could be expected that proximity to the polar X-group would influence the surroundings of the first CH_2 -group. This observation lead to the conclusions that a) contributions from polar groups and H normally are the same whether they are covalently linked to each other or are separated by one or more methylene groups and that the effects thus can be separated using extrapolated values for the compounds with $n=0$, and that b) influences on water structure are of a short-range nature. The latter conclusion is further supported by the fact that branching of alkyl chains has little effect on aqueous $C_{p,2}^\infty$ values.

Two ways of separating functional group contributions are shown in which it is assumed that one type of substituent is equivalent from a hydration point of view independently of its position in the molecule. The set of parameters used in the paper were chosen on the basis of their internal additivity and because parameters derived from α,ω -compounds in paper III are suspected to include other effects than those arising only from solute-solvent interactions. It is found from the values in Table 9 that hydrogen gives a very large positive contribution to aqueous $C_{p,2}^\infty$ values, while polar groups containing atoms of oxygen and nitrogen are near zero or negative.

Table 9. Functional group parameter values ($\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$)

Group	Parameter value	Group	Parameter value	Group	Parameter value
CH_3	157	H	67	$NHCO$	-61
CH_2	90	OH	9	$COOH$	5
CH	23	O	-57	C_6H_5	266
C	-44	NH_2	-2		

The effect of branching was investigated by comparing pairs of compounds of the type PrX , $i-PrX$; BuX , $i-BuX$ and BuX , $t-BuX$. Assuming no influence from the polar groups on the branched alkyl chains and vice versa, it was found that branching $n-$ to $i-$ gives no significant effect while branching $n-$ to $t-$ gives less uniform results. Deviations indicate that the assumption above does not hold for t -branching, but excluding the anomalous value for $t-BuOH$, a mean change in $C_{p,2}^\infty$ of $-30 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ was used when $C_{p,2}^\infty$ values for compounds having tertiary carbon groups were calculated in later sections of the paper.

In a similar treatment it was shown that the loss of two hydrogens can account for the greater part of the decrease in $C_{p,2}^\infty$ observed on cyclization of straight chain molecules.

Internal consistency of the system was shown for the series of compounds included in the derivation of the parameter values. From this comparison it was suggested that the predicted value for heptanol is more reliable than the experimental value and it was found that aqueous $C_{p,2}^{\infty}$ values for diethoxyethane and formamide, which were not included among the compounds on which the system is based, are in good agreement with calculated values.

The system is found especially valuable in estimating $C_{p,2}^{\infty}$ values for hydrocarbons which due to low solubilities in water have been difficult to measure. Calorimetric data are consistent with the system but large deviations are found in values obtained from solubility data. In the aromatic hydrocarbons the CH_2 -increment is very low between benzene and toluene but the higher homologs do conform even if experimental uncertainties are large.

Experimental values for α,ω -difunctional compounds from paper III are substantially lower than predicted values for the higher homologs which suggests that even if temperature dependent internal hydrogen bonding is a primary effect, it is not the only cause of their anomalous behaviour. Steric effects permitting the exclusion of water from contact with hydrophobic parts of the molecule would produce lower $C_{p,2}^{\infty}$ values (cf. reference 31).

With aromatic hydrocarbons having polar substituents CH_2 -increments of about $70 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ are found and predicted $C_{p,2}^{\infty}$ values are significantly lower than experimental values for the lower homologs.

Secondary amines show positive deviations from additivity for the larger compounds and a very large CH_2 -increment ($156 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$) is noted between methyl-ethylamine and diethylamine, while the most positive effects are seen with the lower tertiary amines. Differences between primary, secondary and tertiary amines in their abilities to act as proton donors should be observed when probable causes of the deviations are discussed.

Finally the system was applied to a number of hydroxyl compounds and urea shown in Table 10.

Table 10. Comparison between experimental^a and calculated^b $C_{p,2}^{\infty}$ values for some hydroxy compounds and urea in aqueous solution.

Compound	$C_{p,2}^{\infty}/\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$		Difference
	Experimental	Calculated	
Dimethyl-2,3-propanediol	432.3 ± 0.3	438	-6
1,1,1-Tris(hydroxymethyl)ethane	373.3 ± 0.2	380	-7
Pentaerythritol	328.8 ± 0.2	322	7
Neopentanol	503.5 ± 0.7	496	8
Glycerol	279, 226	230	49, -4
Sucrose	634, 633	281	353, 352
TRIS	405	221	184
Urea	87.5 ± 1	4	84

^aLiterature references see paper V.

^bAssuming a t-branching effect of $-30 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$

Good agreement is found between most experimental and calculated values but large deviations are found for TRIS, sucrose and urea.

The formal nature of the parameter values should be pointed out but it is believed that large deviations from the behaviour of the simple compounds used for the derivation of the system do reveal interesting features in more complex molecules which needs further investigation. Particularly interesting would be to compare aqueous $C_{p,2}^{\infty}$ values for different mono- and disaccharides in the light of a specific hydration model suggested in references 32 and 33, provided effects of mutarotation could be controlled. Additional experimental work to further establish the basis of the system should include series of compounds of the types $RO-(CH_2)_n-OR'$, $RO-(CH_2)_n-OH$, mono- and polyethers to test the assumptions about constant CH_2 - and O-contributions to aqueous $C_{p,2}^{\infty}$ values.

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